

Europäisches Patentamt

European Patent Office

Office européen des brevets



(11)

EP 1 005 872 A1

(12)

EUROPEAN PATENT APPLICATION

(43) Date of publication:
07.06.2000 Bulletin 2000/23

(51) Int. Cl.⁷: **A61L 27/00**, A61L 31/00,
A61L 29/00

(21) Application number: **00200859.7**

(22) Date of filing: **26.04.1994**

(84) Designated Contracting States:
AT BE CH DE DK ES FR GB IE IT LI LU NL PT SE

(30) Priority: **01.06.1993 US 70074**

(62) Document number(s) of the earlier application(s) in
accordance with Art. 76 EPC:
98103006.7 / 0 847 765
94912052.1 / 0 701 453

(71) Applicant:
Stryker Technologies Corporation
Kalamazoo, MI 40992 (US)

(72) Inventors:
• **Sun, Deh Chuan**
Rockaway, NJ 07866 (US)
• **Stark, Casper F.**
Pompton Lakes, NJ 07442 (US)

(74) Representative:
Hammond, Andrew David et al
Göteborgs Patentbyrå Dahls AB,
Sjöporten 4
417 64 Göteborg (SE)

Remarks:

This application was filed on 09 - 03 - 2000 as a
divisional application to the application mentioned
under INID code 62.

(54) **Non-oxidizing polymeric medical implant**

(57) A medical implant comprising an olefinic material having a molecular weight greater than 400,000. The material is irradiated to create free radicals while out of contact with oxygen in a concentration greater than 1% volume by volume and then heated while out of contact with oxygen in a concentration greater than 1% volume by volume at a temperature of greater than 25°C for a sufficient time to create a level of cross-links between free radicals at least equivalent to the level created by heating the olefinic material to 50°C for 144 hours.

EP 1 005 872 A1

Description**BACKGROUND OF THE INVENTION**5 **Field of the Invention**

[0001] This invention relates to medical implants formed of a polymeric material such as ultra-high molecular weight polyethylene, with superior oxidation resistance upon irradiation and a method for making the same.

10 **Description of the Prior Art**

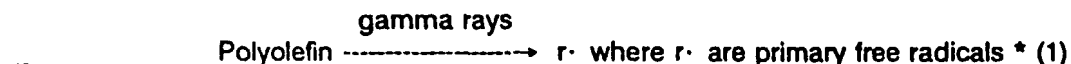
[0002] Various polymer systems have been used for the preparation of artificial prostheses for biomedical use, particularly orthopedic applications. Among them, ultra-high molecular weight polyethylene is widely used for articulation surfaces in artificial knee and hip replacements. Ultra-high molecular weight polyethylene (UHMWPE) has been defined as those linear polyethylenes which have a relative viscosity of 2.3 or greater at a solution concentration of 0.05% at 135°C in decahydronaphthalene. The nominal weight - average molecular weight is at least 400,000 and up to 10,000,000 and usually from three to six million. The manufacturing process begins with the polymer being supplied as fine powder which is consolidated into various forms, such as rods and slabs, using ram extrusion or compression molding. Afterwards, the consolidated rods or slabs are machined into the final shape of the orthopedic implant components.

20 Alternatively, the component can be produced by compression molding of the UHMWPE resin powder.

[0003] All components must then go through a sterilization procedure prior to use, but usually after being packaged. There exists several sterilization methods which can be utilized for medical applications, such as the use of ethylene oxide, heat, or radiation. However, applying heat to a packaged polymeric medical product can destroy either the integrity of the packaging material (particularly the seal, which prevents bacteria from going into the package after the sterilization step) or the product itself.

25 **[0004]** Because ethylene oxide may adversely impact environmental and employee safety, gamma ray, x-ray or electron beam radiation has been utilized as a preferred means of sterilization. These types of radiation use a high energy beam to kill bacteria, viruses, or other microbial species contained in the packaged medical products, achieving the goal of product sterility.

30 **[0005]** However, it has been recognized that regardless of the radiation type, the high energy beam causes generation of free radicals in polymers during radiation. It has also been recognized that the amount of free radicals generated is dependent upon the radiation dose received by the polymers and that the distribution of free radicals in the polymeric implant depends upon the geometry of the component, the type of polymer, the dose rate, and the type of radiation beam. The generation of free radicals can be described by the following reaction (which uses polyolefin and gamma ray irradiation for illustration):

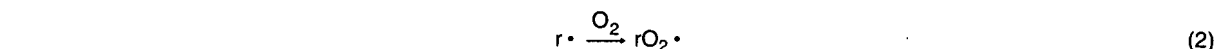


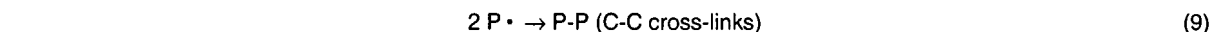
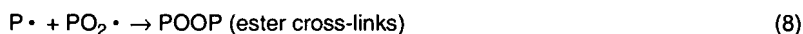
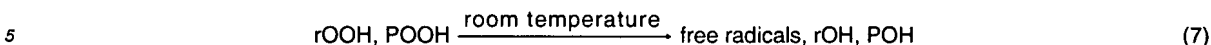
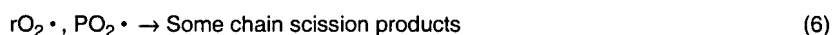
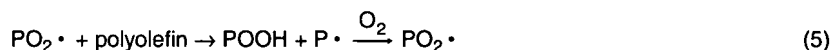
***(through C-C chain scission or C-H scission)**

45 **[0006]** Depending whether or not oxygen is present, primary free radicals $\text{r} \cdot$ will react with oxygen and the polymer according to the following reactions as described in "Radiation Effects on Polymers", edited by Roger L. Clough and Shalaby W. Shalaby, published by American Chemical Society, Washington, D.C., 1991.

50 **In the presence of oxygen**

[0007]





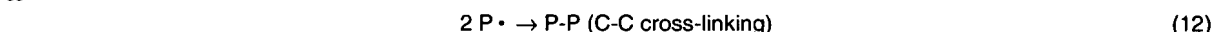
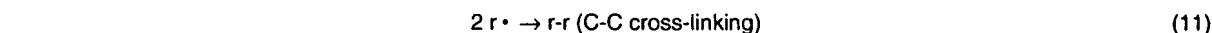
[0008] In radiation in air, primary free radicals $\text{r} \cdot$ will react with oxygen to form peroxy free radicals $\text{rO}_2 \cdot$, which then react with polyolefin (such as UHMWPE) to start the oxidative chain scission reactions (reactions 2 through 6). Through these reactions, material properties of the plastic, such as molecular weight, tensile, and wear properties, are degraded.

[0009] Recently, it was found that the hydroperoxides (rOOH and POOH) formed in reactions 3 and 5 will slowly break down as shown in reaction 7 to initiate post-radiation degradation. Reactions 8 and 9 represent termination steps of free radicals to form ester or carbon-carbon cross-links. Depending on the type of polymer, the extent of reaction 8 and 9 in relation to reactions 2 through 7 may vary. For irradiated UHMWPE, a value of 0.3 for the ratio of chain scission to cross-linking has been obtained, indicating that even though cross-linking is a dominant mechanism, a significant amount of chain scission occurs in irradiated polyethylene.

[0010] By applying radiation in an inert atmosphere, since there is no oxidant present, the primary free radicals $\text{r} \cdot$ or secondary free radicals $\text{P} \cdot$ can only react with other neighboring free radicals to form carbon-carbon cross-links, according to reactions 10 through 12 below. If all the free radicals react through reactions 10 through 12, there will be no chain scission and there will be no molecular weight degradation. Furthermore, the extent of cross-linking is increased over the original polymer prior to irradiation. On the other hand, if not all the free radicals formed are combined through reactions 10, 11 and 12, then some free radicals will remain in the plastic component.

In an Inert Atmosphere

[0011]



It is recognized that the fewer the free radicals, the better the polymer retains its physical properties over time. The greater the number of free radicals, the greater the degree of molecular weight and polymer property degradation will occur. Applicant has discovered that the extent of completion of free radical cross-linking reactions is dependent on the reaction rates and the time period given for reaction to occur.

[0012] Several prior art patents attempt to provide methods which enhance UHMWPE physical properties. European Patent Application 0 177 522 B1 discloses UHMWPE powders being heated and compressed into a homogeneously melted crystallized morphology with no grain memory of the UHMWPE powder particles and with enhanced modulus and strength. U.S. Patent 5,037,928 discloses a prescribed heating and cooling process for preparing a UHMWPE exhibiting a combination of properties including a creep resistance of less than 1% (under exposure to a temperature of 23°C and a relative humidity of 50% for 24 hours under a compression of 1000 psi) without sacrificing tensile and flexural properties. U.K. Patent Application GB 2 180 815 A discloses a packaging method where a medical device which is sealed in a sterile bag, after radiation/sterilization, is hermetically sealed in a wrapping member of oxygen-impermeable material together with a deoxidizing agent for prevention of post-irradiation oxidation.

[0013] U.S. Patent 5,153,039 relates to a high density polyethylene article with oxygen barrier properties. U.S. Patent 5,160,464 relates to a vacuum polymer irradiation process.

SUMMARY OF THE INVENTION

[0014]

The present invention relates to a method for providing a polymeric material, such as UHMWPE, with superior oxidation resistance upon irradiation. For the purpose of illustration, UHMWPE will be used as an example to describe the invention. However, all the theories and processes described hereafter should also apply to other poly-

meric materials such as polypropylene, high density polyethylene, polyester, nylon, polyurethane and poly(methylmethacrylate) unless otherwise stated.

5 [0015] As stated above, while UHMWPE polymer is very stable and has very good resistance to aggressive media except for strong oxidizing acids. Upon sterilization radiation, free radicals are formed which cause UHMWPE to become activated for chemical reactions and physical changes. Possible chemical reactions include reacting with oxygen, water, body fluids, and other chemical compounds while physical changes include density, crystallinity, color, and other physical properties. In the present invention a new sterilization radiation process greatly reduces the adverse effects caused by a conventional radiation process. Furthermore, this new sterilization process does not employ stabilizers, antioxidants, or any other chemical compounds which may have potential adverse effects in biomedical or orthopedic applications.

10 [0016] In the sterilization process of the present invention, a polymeric orthopedic implant component to be sterilized by radiation does not contain oxidants, such as oxygen or water (or moisture), or free radicals. This may be accomplished by obtaining a raw material for the implant manufactured under a special process as described herein and forming a part of the invention.

15 [0017] The finished polymeric orthopedic component is then sealed in an oxidant-free atmosphere. This oxidant-free atmosphere is maintained during radiation. The radiated polymeric component is then subjected to a heat treatment to cross-link all the free radicals within themselves. During this treatment, the condition of oxidant-free atmosphere is maintained. The irradiated, heat treated plastic component is now ready to use. Exposure to oxygen or moisture will not cause oxidation. The oxidation resistance to any oxidizing agent is similar to that of the unirradiated virgin polymer.

20 [0018] It is therefore an object of the invention to provide a polymeric orthopedic implant having superior oxidation resistance after irradiation.

[0019] It is still another object of the invention to provide a method for manufacturing such an implant from the resin powder thereof through the final sterilization step so that the implant may thereafter be exposed to air without degradation due to oxidation.

25 [0020] These and other objects are achieved by a method for producing a polymeric medical implant including the steps of placing the polymeric resin in a sealed container and removing a substantial portion of the oxygen from the container. After a predetermined time, the container is repressurized with an inert gas such as nitrogen, argon, helium or neon. The resin is thereafter transferred to a forming device which normally melts and forms the resin in an oxygen reduced atmosphere to produce a polymeric raw material. The polymeric raw material, such as UHMWPE is then machined to an implant such as a tibial tray or a liner for an acetabular cup. The finished part is then sealed into a package in an oxygen reduced atmosphere. The package is of an air-tight nature to prevent oxygen or moisture from entering after the package is sealed. The then packaged implant is radiation sterilized and then heat treated for the predetermined time and temperature sufficient to form cross-links between free radicals of the neighboring polymeric chains. This prevents further oxidation once the implant is removed from the package.

35 [0021] In general, the implant is heated for at least 48 hours at a temperature of about 37°C to about 70°C and preferably for 144 hours at 50°C.

DESCRIPTION OF THE PREFERRED EMBODIMENT

40 [0022] In the preferred method, a raw polymeric material such as UHMWPE is obtained by, for example, ram extrusion, compression molding, or other forming processes. These methods use virgin polymer powder as a starting material. However, virgin polymer resin powder may contain air or moisture, which may exist in the resin micro-structure or simply deposited on the resin surfaces. If air or moisture is not removed from resin powder prior to the forming process, it can be trapped in the plastic matrix after forming and can not escape. This is true even with the use of vacuum or gas flushing techniques. During the sterilization radiation process, the trapped air or moisture or both will react with free radicals generated in the plastic to cause oxidation. The trapped moisture can also absorb radiation energy and dissociate into oxygen and hydroxyl free radicals which will also react with the plastic to cause oxidation. Therefore, by removing air and moisture prior to the forming process, oxidation during sterilization radiation can be avoided.

50 [0023] The preferred method for eliminating air and moisture is to apply a vacuum of less than 3" of mercury (76 torr) to the polymer resin for a prescribed time to reduce the levels of air and moisture to a minimal or acceptable value. The level for oxygen is preferably 0.5% (volume by volume and no more than 1%). The moisture level is preferably 10% of relative humidity (and no more than 20% relative humidity). Then sufficient amounts of deoxidizing agents, such as oxygen absorbents and moisture desiccants, are placed together with the polymer resin in a sealed container to reduce the levels of air and moisture to the minimal or acceptable value. An example of an oxygen absorbent is AGELESS® which is an iron oxide compound and commercially available from Cryovac Division, W.R. Grace & Co., Duncan, S.C.. An example of moisture desiccant is silica gel which is commercially available. These materials are placed with the resin in the sealed container for approximately 10 hours. Alternately, or in combination, an inert gas, such as nitrogen,

argon, helium or neon is used to flush the container, holding the polymer resin powder, until the levels of air and moisture are reduced to the accepted value. Of course, any combination of the above methods can also be used.

- 5 **[0024]** In order to ensure a raw material for an orthopedic implant with no oxygen, not only must the UHMWPE resin powder be free of air and moisture, but the entire forming operation of, for example, ram extrusion, compression molding, or other forming process should be carried out in an inert or low oxygen atmosphere as well. During the forming process, due to high temperature and high pressure applied in the process, UHMWPE polymer chains may be broken to generate free radicals and cross-links. While cross-links generated in the forming process have no adverse effects on material properties, the free radicals produced, as described above, can react with air or other oxidants. Therefore, it is important to maintain the inert atmosphere during the forming process to minimize oxidation.
- 10 **[0025]** Any free radicals generated should be eliminated as soon as the forming process is completed by annealing. If the formed UHMWPE contains free radicals and is exposed to air or other oxidants after the forming process, oxidation will occur. The polymer should be annealed at an elevated temperature in an inert atmosphere for a prescribed time. This is because the rate of free radical reactions (reactions 10 through 12) increase with increasing temperature, according to the following general expressions:

$$\frac{dr \cdot}{dt} = k_1 [r \cdot] \quad \text{and} \quad \frac{dP \cdot}{dt} = k_2 [P \cdot] \quad (13)$$

- 20 **[0026]** Compared to room temperature, an elevated temperature not only increases the reaction rate constants, k_1 and k_2 , but also helps free radicals $r \cdot$ and $P \cdot$ to migrate in the plastic matrix to meet other neighboring free radicals for cross-linking reactions. In general, the desired elevated temperature is between the room temperature and the melting point of the polymer. For UHMWPE, this temperature range is between about 25°C and about 140°C. However, the preferred annealing temperature range is from about 37°C to about 135°C. The preferred time and temperature is 25 130°C for 20 hours with the minimum annealing time being about 4 hours (requiring a temperature at the high end of the range). It is to be noted that the higher the temperature used, the shorter the time period needed to combine free radicals. Additionally, due to the high viscosity of an UHMWPE melt, the formed UHMWPE often contains residual (internal) stress caused by incomplete relaxation during the cooling process, which is the last step of the forming process. The annealing process described herein will also help to eliminate or reduce the residual stress. A residual stress 30 contained in a plastic matrix can cause dimensional instability and is in general undesirable.

- [0027]** In applications such as for orthopedic implants, the formed UHMWPE is further machined into desired shapes. In general, the machining is done at room temperature and no damage to the plastic will occur. However, certain machine tools, when operated at a high speed, may generate local heat and cause thermal breakdown of UHMWPE polymer chains. In this case, the above described annealing process may be employed to eliminate any 35 newly formed free radicals prior to packaging.

- [0028]** After machining, the polymeric component is packaged in an air tight package in an oxidant-free atmosphere. Thus, all air and moisture must be removed from the package prior to the sealing step. Machines to accomplish this are commercially available, such as from Orics Industries Inc., College Point, New York, which flush the package with a chosen inert gas, vacuum the container, flush the container for the second time, and then heat seal the container 40 with a lid. In general, less than 0.5% (volume by volume) oxygen concentration can be obtained consistently. An example of a suitable oxidant impermeable (air tight) packaging material is polyethylene terephthalate (PET). Other examples of oxidant impermeable packaging material is poly(ethylene vinyl alcohol) and aluminum foil, whose oxygen and water vapor transmission rates are essentially zero. All these materials are commercially available. Several other suitable commercial packaging materials utilize a layer structure to form a composite material with superior oxygen and 45 moisture barrier properties. An example of this type is a layered composite comprised of poly-propylene/poly(ethylene vinyl alcohol)/polypropylene.

- [0029]** In general, the sterilization radiation step for the packaged implant may take a few hours to complete. As described above, it is imperative that during this time period, the transmission of oxidants, such as oxygen and moisture, into the package be kept to a minimal or at an acceptable value to avoid oxidation.

- 50 **[0030]** Following sterilization radiation, a heat treatment step should be performed in an inert atmosphere and at an elevated temperature to cause free radicals to form cross-links without oxidation. If proper packaging materials and processes are used and oxidant transmission rates are minimal, then the oxidant-free atmosphere can be maintained in the package and a regular oven with air circulation can be used for heat treatment after sterilization. To absolutely ensure that no oxidants leak into the package, the oven may be operated under a vacuum or purged with an inert gas.
- 55 In general, if a higher temperature is used, a shorter time period is required to achieve a prescribed level of oxidation resistance and cross-linking. In many cases, the relationship between the reaction temperature and the reaction rate follows the well-known Arrhenius equation:

$$k_1 \text{ or } k_2 = A \cdot \exp (\Delta H/T) \quad (14)$$

where

- 5 k_1 and k_2 are reaction rate constants from reactions 13 and 14
 A is a reaction dependent constant
 ΔH is activation energy of reaction
 T is absolute temperature (K)

10 **[0031]** However, the temperature should not exceed the distortion temperature of either the packaging material or the plastic components. For UHMWPE, the temperature range is between about 25°C and about 140°C. However, considering the distortion of the packaging material, the preferred temperature is 37°C to 70°C.

[0032] It is very important to ensure that the number of free radicals has been reduced to a minimal or an accepted level by the heat treatment. This is because the presence of an oxidant causes not only the oxidation of pre-existing free radicals, but also the formation of new free radicals via reactions 2 through 7. When the number of free radicals grows, the extent of oxidation and the oxidation rate will increase according to the following equations:

$$\frac{dr \cdot}{dt} = k_3 [r \cdot][O_2] \quad \text{and} \quad \frac{dP \cdot}{dt} = k_4 [P \cdot][O_2] \quad (15)$$

20

[0033] Where free radicals $r \cdot$ and $P \cdot$ can grow in number in the presence of oxidants and in turn increase the oxidation rates. It is also to be noted that the oxidation reaction rate constants k_3 and k_4 increase with increasing temperature, similar to k_1 and k_2 . Therefore, to determine if a certain level of residual free radicals is acceptable or not, it is required to evaluate specific material properties after the plastic sample is stored or aged at the application temperature for a time period which is equal to or longer than the time period intended for the application of the plastic component. An alternative to the method to assess the aging effect is to raise the aging temperature of the plastic sample for a shorter time period. This will increase the reaction rate constants k_3 and k_4 significantly and shorten the aging time. It has been found that an acceptable level of residual free radicals is $1.0 \times 10^{17}/g$ for UHMWPE use for orthopedic implants.

30 **[0034]** After heat treatment, the irradiated packaged plastic component is now ready to use. The package can be opened and exposed to air or moisture without causing oxidation. The oxidation resistance of the sterilized plastic component to other oxidants is similar to that of the virgin, unirradiated polymer.

35 Sample Preparation

[0035] A surgical grade UHMWPE rod produced by ram extrusion was machined into samples of desirable shapes. Four sets of samples were prepared using these machined samples by the following methods:

- 40 Method A: an UHMWPE sample as machined and unirradiated
 Method B: An UHMWPE sample was heat sealed in a glycol-modified polyethylene terephthalate (PETG, made by Eastman Plastics, Inc., Kingsport, Tennessee) blister in air with an aluminum lid of 0.1 mm in thickness. The sealed blister containing the UHMWPE sheet was sterilized by irradiation of gamma-rays in a dose of 2.5 Mrad. The package was then opened and exposed to room air.
- 45 Method C: An UHMWPE sample was placed in a PETG blister and heat sealed in dry nitrogen with an aluminum lid of 0.1 mm in thickness by the Orics Vacuum Gas Flush Heat Seal Machine (Model SLS-VGF-100M for modified atmosphere packaging, made by Orics Industries Inc., College Point, New York.) which went through the following cycles:
- 50 i) nitrogen gas (moisture-free) flush for five seconds
 ii) vacuum to a pressure of equal to or below 3 inches of mercury
 iii) nitrogen gas flush (moisture-free) for five seconds
 iv) heat seal

55 The oxygen concentration in the sealed blister was measured by a Mocon Oxygen Analyzer to be 0.325% (volume by volume). The sealed blister containing the UHMWPE sample was sterilized by irradiation of gamma-rays in a dose of 2.5 Mrad. The oxygen concentration in the sealed blister after sterilization radiation was measured to be 0.350%. The package was then opened and exposed to room air.

Method D: Same as Method C, except that after gamma-ray irradiation, the sealed blister containing the UHMWPE sample was heat treated at 50°C for 144 hours in an oven, then transferred from the oven to room temperature for cooling. After the package was cooled to room temperature, the oxygen concentration was measured by a Mocon Oxygen Analyzer to be 0.360%. The package was then opened and exposed to room air.

[0036] Samples prepared by the above methods were used in the following examples for evaluation.

Example 1:

[0037] Two sets of 1-mm-thick UHMWPE sheets prepared by Methods A through D above were oven aged in air at 80°C for 11 and 23 days respectively. After these sheets were cooled in room temperature, a thin film specimen of about 100 microns in thickness was cut from each of the 1-mm-thick aged UHMWPE sheets and placed in an IR window for a standard FTIR (A Nicolet 710 FTIR system was used) transmission run. A total of 32 spectra (scans) were collected and averaged. To determine the extent of oxidation, the IR absorption peaks in the frequency range of between 1660 and 1800 cm^{-1} , corresponding to carbonyl (C=O) functional groups, were integrated for the peak area. The peak area is proportional to the amount of oxidized UHMWPE in the specimen. To correct for difference in specimen thickness, the integrated peak area was then normalized to the specimen thickness, by dividing by the area of the 1463 cm^{-1} (methyl) peak which is proportional to the specimen thickness. The obtained ratio was defined as oxidation index. A third set of 1-mm-thick UHMWPE sheets prepared by methods A through D, but without oven aging, were also evaluated by the same FTIR method for comparison. Oxidation indices obtained are shown in Table 1:

TABLE 1

Sample	Oxidation Index
Method A / not oven aged	ca. 0.
Method A / 11 day oven aging	ca. 0.
Method A / 23 day oven aging	ca. 0.
Method B / not oven aged	0.02
Method B / 11 day oven aging	0.06
Method B / 23 day oven aging	0.11
Method C / not oven aged	0.01
Method C / 11 day oven aging	0.04
Method C / 23 day oven aging	0.08
Method D / not oven aged	0.01
Method D / 11 day oven aging	0.01
Method D / 23 day oven aging	0.01

[0038] From Table 1 results, it can be seen that the unirradiated UHMWPE sample (Method A) was free of oxidation (below the FTIR detectable level), even after 23 days of oven aging in air at 80°C. On the other hand, the UHMWPE sample irradiated in air (Method B) showed considerable oxidation and the extent of oxidation (as indicated by the oxidation index) increased with increasing aging time. After 23 days of oven aging, the oxidation index reached 0.11. For the UHMWPE sample irradiated in nitrogen (Method C), the initial oxidation index before oven aging was 0.01 which was not significant. However, during the oven aging, the oxidation index increased to 0.04 for 11 days and 0.08 for 23 days respectively. The results indicate that while irradiation in an inert atmosphere is an improvement over oxidation in air, the irradiated plastic component will oxidize further over time once it is exposed to air or other oxidants. In contrast, the UHMWPE sample irradiated in nitrogen followed by heat treatment at 50°C for 144 hours (Method D), showed an initial

oxidation index of only 0.01 which did not increase after 11 or 23 days of oven aging, indicating that this sample has superior oxidation resistance than the samples prepared by Method B or C.

Example 2:

[0039] Two sets of 1-mm-thick UHMWPE sheets prepared by Methods B through D cited in the Sample Preparation were oven aged in air at 80°C for 11 and 23 days respectively. After these sheets were cooled in room temperature, six tensile specimens with a dumbbell shape according to ASTM D638 (Type IV) were cut from each of the 1-mm-thick aged UHMWPE sheets. A standard tensile test was performed for each specimens at a speed of 2 inches/min. Another set of 1-mm-thick UHMWPE sheets prepared by Methods B through D cited in the Sample Preparation, but without oven aging, were also evaluated by the same tensile test method for comparison. Tensile breaking strength results (average of six tests for each condition) are shown in Table 2:

TABLE 2

Sample	Tensile Breaking Strength, psi
Method B / not oven aged	6510
Method B / 11 day oven aging	5227
Method B / 23 day oven aging	3192
Method C / not oven aged	6875
Method C / 11 day oven aging	6400
Method C / 23 day oven aging	6004
Method D / not oven aged	6941
Method D / 11 day oven aging	7113
Method D / 23 day oven aging	6904

[0040] From Table 2, tensile breaking strength shows the most deterioration for the sample irradiated in air (Method B). The sample irradiated in nitrogen (Method C) shows some improvement over the sample prepared by Method B. However, the decrease in tensile breaking strength upon oven aging still occurs. In contrast, the sample irradiated in nitrogen followed by heat treatment (50°C for 144 hours, Method D), shows no change in tensile breaking strength, indicating a superior oxidation resistance.

Example 3:

[0041] Two sets of 1-mm-thick UHMWPE sheets prepared by Methods B and Method D cited in the Sample Preparation were oven aged in air at 80°C for 11 and 23 days respectively. After these sheets were cooled in room temperature, samples cut from sheets were characterized by a high temperature gel permeation chromatograph (GPC) column for molecular weight distribution. The samples were dissolved in hot trichlorobenzene (TCB). They were then run in the aforementioned solvent at 1.2 ml/min. using a Jordi Gel Mixed Bed Column, 50cm x 10.0mm ID., at a column oven temperature of 145°C on the Waters 150C Chromatograph. The injection size was 250uL of a 0.1% solution. An antioxidant (N-phenyl-2-naphthylamine) was added to all high temperature GPC samples to prevent polymer deterioration.

[0042] Prior to sample runs, the column was calibrated using narrow MW polystyrene standards. Since the samples were only partially soluble in the solvent due to cross-linking, the so-determined molecular weight distribution was for the soluble portion only. To determine the extent of cross-linking (solubility), a two hundred milligram sample cut from sheets were dissolved in 100cc of 1,2,4-trichlorobenzene. Each sample was then heated to approximately 170°C with N-phenyl-2-naphthylamine antioxidant added for 6 hours. The samples were then hot filtered at approximately 170°C using separate preweighed high temperature filters for each sample.

[0043] After filtration, the filters were cooled to room temperature and washed individually with dichloromethane.

They were then placed in a convection oven at 105°C for 6 hours to dry and then reweighed. The weight fraction of the undissolved (cross-linked) portion was then determined based upon the initial weight of 200 mg. To determine the low molecular weight fraction present in each sample, the weight fraction of molecular weight below 10^5 in the soluble portion, determined by GPC, was multiplied by the percent solubility to give weight percent of low molecular weight fraction in each sample. Results are shown in Table 3:

TABLE 3

Sample	Weight Percent of Soluble Portion Below 10^5	Percent Solubility in Solvent	Weight Percent of Entire Sample Below 10^5
Method B /without oven aging	28.0	98.2	27.5
Method B/11 day oven aging	36.2	100.0	36.2
Method B /23 day oven aging	48.1	100.0	48.1
Method D /without oven aging	22.7	80.9	18.4
Method D/11 day oven aging	20.5	73.6	15.1
Method D /23 day oven aging	24.2	74.7	18.1

[0044] From Table 3, it can be seen that the sample made by Method D contains more cross-linking (i.e. less soluble) than one made by Method B. Upon oven aging, the low molecular weight fraction (defined as below 10^5) in the sample made by Method B increases from 0.275 to 0.481 while that of the sample made by Method D remains virtually unchanged at about 0.18 after 23 days of oven aging. The increase in low molecular weight fraction was due to chain scission caused by oxidative reactions. The results indicate that the process of method D can produce an irradiated polymer with a superior oxidation resistance.

Example 4:

[0045] UHMWPE samples of 0.5 inch cubes prepared by Methods B and Method D cited in the Sample Preparation were evaluated for deformation under load (creep resistance). Testing procedures according to ASTM D 621 (A) (24hr/23°C/1000 psi/90 min recovery) were used. Results are summarized in Table 4:

TABLE 4

Sample	Deformation under Load, %
Method B	0.80
Method D	0.60

[0046] From Table 4, it is concluded that the sample prepared by Method D, the invention, possesses a superior creep resistance (0.6%) to one prepared by Method B (0.8%).

Example 5:

[0047] Two 1-mm-thick UHMWPE samples were annealed in a oven filled with air and dry nitrogen (oxygen concentration is below 0.2%) respectively at 130°C for 20 hours in order to remove residual stress on the samples. After the sheets were cooled to room temperature in the oven, they were removed from the oven and cut into dumbbell shaped tensile specimens (ASTM D 638, Type V) for evaluation. A standard tensile test according to ASTM D 638 was performed at a speed of 2 inches/min for each of six specimens annealed in air and in dry nitrogen respectively. Results are shown in Table 5:

TABLE 5

Sample	EAB, %	TYS, psi	TBS, psi	Toughness, lbs-in/in ³
Air annealed	414	3547	6257	10,210
Nitrogen annealed	485	3517	8917	18,960
Note: EAB - elongation at break TYS - tensile yield strength TBS - Tensile breaking strength				

[0048] From the above table, it is seen that the sample annealed in nitrogen exhibits a higher elongation at break, a higher tensile breaking strength, and a higher toughness, compared to one annealed in air, while the tensile yield strength is similar between the two samples. The results indicate that the sample annealed in nitrogen is more ductile than the one annealed in air. The loss of ductility in the sample annealed in air is due to oxidative chain scission.

[0049] To determine oxidation indices in these two samples, a thin film specimen of ca. 100 microns in thickness was cut from each of the 1-mm-thick annealed UHMWPE sheets and placed in an IR window for a standard FTIR (a Nicolet 710 FTIR system was used) transmission run, using the procedures and calculations employed in the Sample Preparation. Oxidation indices obtained are shown in Table 6.

TABLE 6

Sample	Oxidation Index
Air Annealed	0.10
Nitrogen Annealed	ca. 0.0

[0050] From the above results, it is seen that the UHMWPE sample annealed in air after ram extrusion showed significant oxidation due to free radicals generated in the forming process. In contrast, the UHMWPE sample annealed in nitrogen showed no oxidation (below the FTIR detectable level). It is concluded that annealing in nitrogen can prevent the polymer from oxidation and produce a polymer with superior ductility.

[0051] While several examples of the present invention have been described, it is obvious that many changes and modifications may be made thereunto, without departing from the spirit and scope of the invention.

Claims

1. A medical implant comprising an olefinic material having a molecular weight greater than 400,000, said material irradiated to create free radicals while out of contact with oxygen in a concentration greater the 1% volume by volume and then heated while out of contact with oxygen in a concentration greater than 1% volume by volume at a temperature of greater than 25°C for a sufficient time to create a level of cross-links between free radicals at least equivalent to the level created by heating said olefinic material to 50°C for 144 hours.
2. The medical implant as claimed in claim 1, wherein said free radicals include peroxy and hydroperoxy groups on the polymer chain.
3. The medical implant as claimed in claim 1 or 2, wherein said irradiating is electron beam irradiation.
4. The medical implant as claimed in any of the preceding claims, wherein the olefinic material is ultra high molecular weight polyethylene.
5. The medical implant as claimed in any of the preceding claims, wherein the olefinic material is surrounded by a layer of material whose function is to prevent said olefinic material from contact with oxygen and said layer is heated while surrounded by an oxygen containing atmosphere.
6. The medical implant as claimed in any of the preceding claims, wherein said olefinic material is heated at a tem-

perature between 25°C and the melting point of the material to form crosslinks.

- 5 7. A medical implant comprising an olefinic material having a molecular weight greater than 400,000 said material irradiated to create free radicals while sealed by a layer of material whose function is to prevent said olefinic material from contact with oxygen in a concentration greater than 1% by volume by volume and then heated at a temperature of greater than 25°C for sufficient time to create cross-links between free radicals while sealed within said layer, wherein the level of cross-linking produced by heating at said temperature and time is equivalent at least to that produced by heating at 50°C for 144 hours.
- 10 8. A medical implant comprising a formed olefinic material having a molecular weight greater than 400,000, said material irradiated to create free radicals while sealed by a layer of material whose function is to prevent said olefinic material from contact with oxygen in a concentration greater than 1% by volume by volume and then heated at a temperature of greater than 25°C for a sufficient time to create cross-links between free radicals while sealed within said layer, wherein the temperature and time is defined by Arrhenius' equation at least as equivalent to the cross-linking produced by heating the olefinic material to 50°C for 144 hours.
- 15 9. The medical implant as claimed in claim 7 or 8, wherein the layer of material whose function is to prevent said olefinic material from contact with oxygen is heated while surrounded by an oxygen containing atmosphere.
- 20 10. A medical implant comprising an olefinic material having a molecular weight greater than 400,000, said material irradiated to create free radicals while out of contact with oxygen in a concentration greater than 1% volume by volume and then heated while out of contact with oxygen in a concentration greater than 1% volume by volume at a temperature greater than 25°C for a sufficient time to create cross-links between free radicals, wherein the temperature and time is defined by Arrhenius' equation as equivalent to at least the cross-linking produced by heating the olefinic material at 50°C for 144 hours.
- 25 11. The medical implant as set forth in claim 10, wherein the olefinic material is surrounded by a layer of material whose function is to prevent said olefinic material from contact with oxygen and said layer is heated while surrounded by an oxygen containing atmosphere.
- 30 12. The medical implant as claimed in any one of the preceding claims, wherein the heating is at least four hours.
13. The medical implant as claimed in any of the preceding claims, wherein the irradiation is a high energy beam of a dose capable of killing bacteria, viruses, or other microbial species.
- 35 14. The medical implant as claimed in any of the preceding claims, wherein said heating has an upper temperature limit of the melting point of the olefinic material.
15. The medical implant as claimed in any of the preceding claims, wherein said olefinic material is heated at a temperature from about 37°C to the melting point of the material.
- 40 16. The medical implant as claimed in any one of claims 1 to 13, wherein said heating has an upper limit not exceeding the distortion temperature of the olefinic material.
- 45
- 50
- 55



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 00 20 0859

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
D,A	EP 0 376 503 A (E.I. DU PONT DE NEMOURS AND CO.) 4 July 1990 (1990-07-04) * claims * & US 5 153 039 A (IDEM) ---	1	A61L27/00 A61L31/00 A61L29/00
A	EP 0 373 800 A (E.I. DU PONT DE NEMOURS AND CO.) 20 June 1990 (1990-06-20) * examples 1-13 * ---	1	
D,A	EP 0 218 003 A (NISSHO CORP.) 15 April 1987 (1987-04-15) * the whole document * & GB 2 180 815 A (IDEM) -----	1	
			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
			A61L
The present search report has been drawn up for all claims			
Place of search THE HAGUE		Date of completion of the search 5 April 2000	Examiner ESPINOSA, M
<p>CATEGORY OF CITED DOCUMENTS</p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document</p>			

EPO FORM 1503 03/92 (P4/C01)

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 00 20 0859

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

05-04-2000

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0376503 A	04-07-1990	AT 122901 T	15-06-1995
		CA 2004455 A	02-06-1990
		DE 68922863 D	29-06-1995
		DE 68922863 T	23-11-1995
		DK 104291 A	31-05-1991
		EP 0449878 A	09-10-1991
		ES 2073012 T	01-08-1995
		JP 4502024 T	09-04-1992
		WO 9006140 A	14-06-1990
		US 5037928 A	06-08-1991
EP 0373800 A	20-06-1990	AT 138810 T	15-06-1996
		CA 2004454 A	02-06-1990
		DE 68926624 D	11-07-1996
		DE 68926624 T	02-10-1996
		DK 57795 A	19-05-1995
		DK 104391 A	31-05-1991
		EP 0446300 A	18-09-1991
		ES 2087147 T	16-07-1996
		JP 4502028 T	09-04-1992
		WO 9006139 A	14-06-1990
		US 5478906 A	26-12-1995
		US 5684124 A	04-11-1997
		US 5621070 A	15-04-1997
EP 0218003 A	15-04-1987	JP 1872208 C	26-09-1994
		JP 4070023 B	09-11-1992
		JP 62074364 A	06-04-1987
		CN 1014863 B	27-11-1991
		DK 184286 A,B,	28-03-1987
		ES 554273 D	01-12-1988
		ES 8900091 A	16-02-1989
		FR 2587977 A	03-04-1987
		GB 2180815 A,B	08-04-1987
		IT 1204329 B	01-03-1989
		SE 500074 C	11-04-1994
		SE 8601776 A	28-03-1987
		US 4813210 A	21-03-1989

EPO FORM P4439

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82